Epithelioid hemangioendothelioma of the common femoral vein: Case report and review of the literature

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A young competitive skier had venous claudication. A stenosis of the left common femoral vein was revealed by means of an examination. Exploration and vein patch angioplasty were performed, and because of both the unusual appearance (focal thickening of vein wall) and the unclear etiology of the lesion, frozen and permanent sections of the wall were obtained. Epithelioid hemangioendothelioma, a rare intravascular sarcoma, was revealed by means of an examination of the permanent sections. Two additional procedures were required to completely excise the epithelioid hemangioendothelioma. We discuss these rare vascular malignancies and include a review of the available literature. Also, oncologic principles important in both the diagnosis and therapy of intravascular sarcomas are discussed. (J Vasc Surg 2001;33:1100-3.)

The practicing vascular surgeon most frequently encounters atherosclerosis and its complications. Unusual vascular pathologies introduce unique clinical and technical challenges. Operations for venous thrombosis, obstruction, or both are uncommon. Likewise, vascular intervention for malignancy is rarely needed, representing two ends of the clinical spectrum. Most commonly, large tumors, such as sarcomas, require resection of vascular structures (eg, vena cava, aorta) as part of a definitive cancer operation.[1-3] These procedures are usually performed in conjunction with an oncologic surgeon. The diagnosis of malignancy is never in doubt, and the issue for the vascular surgeon is the technical reconstruction. Tumors of vascular origin are rarely encountered. Often, these tumors are diagnosed postoperatively, after vascular reconstructions have been performed to relieve obstruction from a presumed benign cause. This report describes a patient whose case illustrates several dilemmas presented by a rare venous tumor, an epithelioid hemangioendothelioma.

CASE REPORT

A 23-year-old man who was a competitive skier reported gradual left leg swelling for several months. This was associated with diffuse leg pain and fatigue with exercise. He had no significant past medical problems. Marked edema of the left lower extremity from the foot to the groin was demonstrated by means of a physical examination. Elevated left common femoral vein velocity (150 cm/s) and turbulence, suggesting a possible arteriovenous communication, was revealed by means of a venous duplex examination. The results of an abdominal computed tomography (CT) scan were normal. Focal stenosis of the left common femoral vein at the inguinal ligament (Fig 1) with a 6-mm pressure gradient at rest was shown demonstrated by venography. There was no evidence of intrinsic or extrinsic mass. The preoperative diagnosis was venous claudication caused by a benign stricture, presumably related to repetitive trauma from competitive skiing (similar to the endofibrosis of the external iliac artery reported in athletes[4-9]).

During surgery, a 2-cm long area of the thickened anterior wall of the common femoral vein was encountered. A longitudinal venotomy was performed at this location. Because of the focal thickening of the vein wall and the unusual preoperative diagnosis, a segment of the wall was sent for frozen section. The diagnosis, made by examination of the frozen section, was chronic thrombosis with minimal cellular atypia. A long vein patch angioplasty was performed by the use of ipsilateral greater saphenous vein, and an arteriovenous fistula was created. Patency of the reconstruction was confirmed by intraoperative venography (Fig 2).

Postoperatively, a prompt resolution of edema occurred in the ipsilateral extremity. However, an epithelioid hemangioendothelioma was demonstrated in the final pathology report, including extramural expert consultation, (Fig 3). Although the patient's chest radiograph appeared normal, two 1-cm peripheral lung nodules were demonstrated by means of a subsequent chest CT scan. Restenosis at the site of patch angioplasty, which coincided with recurrent ipsilateral lower-extremity edema, was demonstrated in a postoperative venous duplex scan at 8 weeks.

At reoperation, a 3-cm long segment of left common femoral/distal external iliac vein was resected with interposition spiral saphenous vein graft. The arteriovenous fistula was left intact. Both resection margins were indicated by examination of the frozen section to be free of tumor. However, a positive caudal margin was revealed by examination of the permanent sections. The patient then underwent a third operation and resection of an additional 3-cm long common femoral vein and interposition contralateral spiral saphenous vein graft. Tumor-free margins were demonstrated by examination of the permanent sections. This final operation resulted in lymphocele requiring reopera-

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Competition of interest: nil.

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Fig 1. Preoperative venogram demonstrating stenosis of the left common femoral vein (*arrow*).

Fig 2. Intraoperative venogram demonstrating widely patent patch angioplasty site (*arrow*).

tion/oversewing. The remainder of the postoperative course was unremarkable.

At 18 months postoperatively, the graft was demonstrated to remain patent without restenosis by means of a duplex scan. The left lower extremity was less than 1 cm larger in circumference than the right without compressive hosiery. Unchanged lung nodules were demonstrated by another chest CT scan. The patient returned to normal athletic activities and competitive sports. If a restenosis develops in the graft, we plan to sample the area by using endovascular methods to determine whether the stenosis is benign or malignant.

DISCUSSION

Malignancy of vascular origin is extremely uncommon, and tumors of nonvascular origin that invade vascular structures are usually large, making the preoperative diagnosis fairly obvious. Primary vascular tumors are frequently malignant sarcomas, such as leiomyosarcomas.[10,11] They are more likely to involve veins than arteries, and most occur in large vessels. As is recommended for the treatment of sarcomas, complete surgical resection (with 2-3 cm margins) offers the best chance for cure.

Sarcomas arising in blood vessels present many potential diagnostic and management challenges. Often, it is impossible to differentiate benign from malignant tumors in the operating room. As illustrated by our case, frozen sections and needle biopsies are notoriously inaccurate when not examined by an experienced multidisciplinary team.[12,13] The histologic nuances of these extremely rare tumors frequently delay the final pathologic diagnosis while numerous pathologists examine slides. The operative plan is markedly different for a benign versus a potentially malignant process, each of which may cause intraluminal vascular obstruction. Most of these points are illustrated by this case. An intraoperative diagnosis of malignancy was not made. A long delay in the final postoperative diagnosis occurred because of the unusual pathology and requirement for consultation. Moreover, the patient ultimately required multiple procedures to excise the lesion completely.

Epithelioid hemangioendothelioma is a rare malignancy of vascular origin.[14-26] To date, 33 total cases have been reported in the English-language literature. The tumor is usually venous in origin (frequently, the femoral vein). It can occur within soft tissues or organ parenchyma. Sex distribution is equal, and the age of onset varies greatly. Histologically, nests or cords of round to spindle-shaped endothelial cells are seen. Despite traditional markers of malignancy including cellular pleomorphism, increased numbers of mitotic figures, and large size, the behavior of individual lesions is unpredictable.[27] Adjuvant chemotherapy, radiation therapy, or both have no proven benefit. Thirty percent of these tumors will develop metastases (half to regional lymph nodes and half to the lungs) that may not appear for many years. Moreover, patients may survive despite metastases because

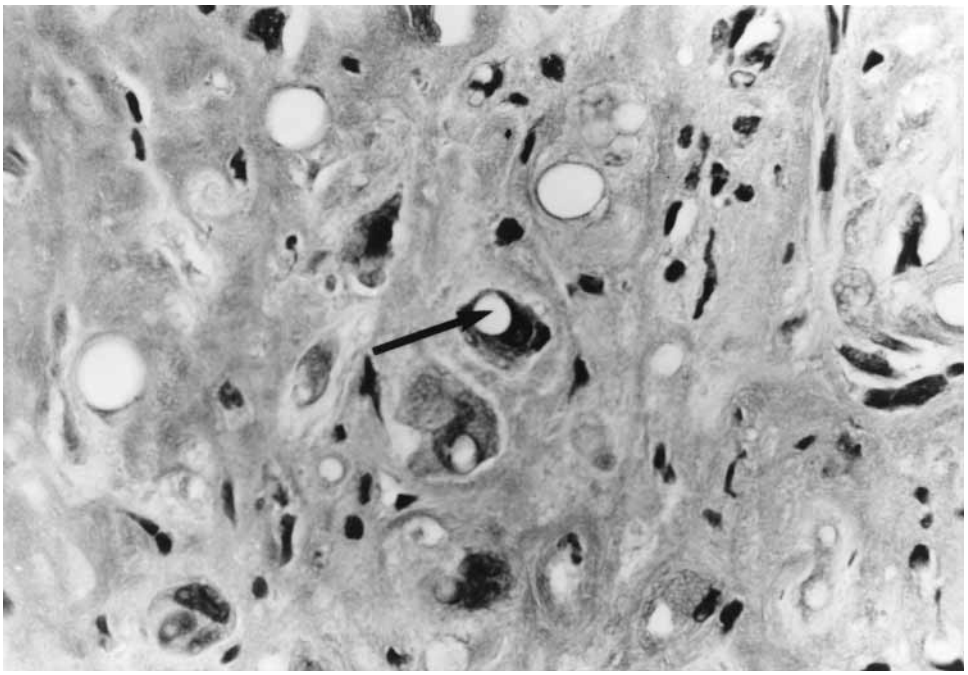

Fig 3. Epithelioid hemangioendothelioma demonstrating plump epithelioid cells with intracytoplasmic, perinuclear "vacuoles" representing miniature lumina (*arrow*) within a hyalinized stroma (hematoxylin and eosin, original magnification × 1000).

of their slow growth, the potential for metastatic lesion resection, or both.[21,22] The overall mortality rate in reported series is less than 20% at 3 to 5 years.[14] Lung lesions are excised when they are more than 1 cm in diameter or when they are found to be enlarging by means of serial CT scan examinations.

How can the treatment of these uncommon tumors be improved? An extremely busy vascular surgeon may see only one of these cases in a lifetime. Surgical therapy for the exceedingly uncommon malignant intravascular pathology is markedly different from more frequently encountered benign problems. Both malignant and benign tumors may demonstrate the same preoperative images and hemodynamic changes. Intravascular tumors often arise in veins, and surgery for benign venous obstruction is uncommon, particularly with the increased efficacy of endovascular methods of therapy. When surgery for venous obstruction is contemplated, most lesions encountered will be benign in nature. However, when an open procedure is performed, it would appear prudent to send a portion of the vascular tissue to pathology in an attempt to detect the rare malignant lesion. Most important, when suspicion of malignancy arises intraoperatively, oncologic surgical consultation is recommended to avoid compromise of oncologic surgical principles before definitive pathologic diagnosis. Adherence to this principle at the time of the second operation may have prevented a third operation in the case presented. Although frozen section may miss marginally malignant lesions like epithelioid hemangioendothelioma because of artifact or interpretive error, it will more reliably identify the more common and more lethal leiomyosarcoma or angiosarcoma.

REFERENCES

1. Hosokawa Y, Matsuge S, Murakami Y, Satoh K, Yamakawa S, Ishigooka M, et al. [Superior vena cava reconstruction combined with resection of mediastinal-pulmonary malignant tumors]. Kyobu Geka 1999;52:25-9.
2. Larsson S, Lepore V. Technical options in reconstruction of large mediastinal veins. Surgery 1992;111:311-7.
3. Fujisawa T, Yamaguchi Y, Nakagawa Y, Yamakawa H, Saitoh H, Saitoh Y, et al. [Reconstruction of superior vena cava with EPTFE graft in cases of invasive superior and anterior mediastinal neoplasms]. Nihon Kyobu Shikkan Gakkai Zasshi 1988;26:145-50.
4. Gallegos CR, Studley JG, Hamer DB. External iliac artery occlusion—another complication of long distance running? Eur J Vasc Surg 1990;4:195-6.
5. Abraham P, Saumet JL, Chevalier JM. External iliac artery endofibrosis in athletes. Sports Med 1997;24:221-6.
6. Abraham P, Chevalier JM, Loire R, Saumet JL. External iliac artery endofibrosis in a young cyclist. Circulation 1999;100:e38.
7. Abraham P, Chevalier JM, Saumet JL. External iliac artery endofibrosis: a 40-year course. J Sports Med Phys Fitness 1997;37:297-300.
8. Abraham P, Saumet JL, Chevalier JM. External iliac artery endofibrosis in athletes. Sports Med 1997;24:221-6.
9. Abraham P, Leftheriotis G, Bourre Y, Chevalier JM, Saumet JL. Echography of external iliac artery endofibrosis in cyclists. Am J Sports Med 1993;21:861-3.
10. van Gulik TM, Taat CW, Slors JF, Bras J, Blank LE, Bakker PJ, et al. Leiomyosarcoma of large and small veins: clinical findings and results of treatment in six patients. Eur J Surg Oncol 1991;17:125-34.
11. Gonzalez EB. Leiomyosarcoma of iliac and femoral veins. Arch Surg 1965;91:623-4.
12. Barth RJ Jr, Merino MJ, Solomon D, Yang JC, Baker AR. A prospec-

tive study of the value of core needle biopsy and fine needle aspiration in the diagnosis of soft tissue masses. Surgery 1992;112:536-43.
13. Heslin MJ, Lewis JJ, Woodruff JM, Brennan MF. Core needle biopsy for diagnosis of extremity soft tissue sarcoma. Ann Surg Oncol 1997;4:425-31.
14. Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer 1982;50:970-81.
15. Ferretti GR, Chiles C, Woodruff RD, Choplin RH. Epitheliod hemangioendothelioma of the superior vena cava: computed tomography demonstration and review of the literature. J Thorac Imaging 1998;13:45-8.
16. Suster S, Moran CA, Koss MN. Epithelioid hemangioendothelioma of the anterior mediastinum: clinicopathologic, immunohistochemical, and ultrastructural analysis of 12 cases. Am J Surg Pathol 1994;18:871-81.
17. Reix T, Sevestre H, Sevestri-Pietri MA, Szychta P, Pietri J. Primary malignant tumors of the venous system in the lower extremities. Ann Vasc Surg 1998;12:589-96.
18. Lau H, Cheng SW. External jugular varix with an intravascular hemangioendothelioma. Surgery 1998;123:359-61.
19. Phookan G, Davis AT, Holmes B. Hemangioendothelioma of the cavernous sinus: case report. Neurosurgery 1998;42:1153-5.
20. Traverse JH, Lesser JR, Flygenring BP, Bracken TH, Olevsky OM, Nicoloff DM, et al. Epithelioid hemangioendothelioma of the thoracic aorta resulting in aortic obstruction and congestive heart failure. Circulation 1999;100:564-5.
21. Enzinger FM, Weiss SW. Hemangioendothelioma: vascular tumors of intermediate malignancy. In: Enzinger FM, editor. Soft tissue tumors. St Louis: Mosby; 1995. p. 627-40.
22. Palsson B. Epitheloid hemangioendothelioma. Acta Oncol 1999;38:659-61.
23. Delin A, Johansson G, Silfversward C. Vascular tumors in occlusive disease of the iliac-femoral vessels. Eur J Vasc Surg 1990;4:539-42.
24. Fischer MG, Gelb AM, Nussbaum M, Haveson S, Ghali V. Primary smooth muscle tumors of venous origin. Ann Surg 1982;196:720-4.
25. Ignacio EA, Palmer KM, Mathur SC, Schwartz AM, Olan WJ. Epithelioid hemangioendothelioma of the lower extremity. Radiographics 1999;19:531-7.
26. Vartanian RK. Epithelioid hemangioendothelioma [letter]. Am J Surg Pathol 1995;19:974.
27. Chen KT. Cytology of epithelioid hemangioendothelioma [letter; comment]. Diagn Cytopathol 1996;14:187-8.

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